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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,184	11/28/2001	Luis Z. Avila	5181	3918

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GENZYME CORPORATION  
LEGAL DEPARTMENT  
15 PLEASANT ST CONNECTOR  
FRAMINGHAM, MA 01701-9322

EXAMINER

DINOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/996,184	<b>Applicant(s)</b> AVILA ET AL.	
	<b>Examiner</b> Liliana Di Nola-Baron	<b>Art Unit</b> 1615	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 February 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

Receipt of Applicant's amendment, filed on February 24, 2004, is acknowledged.

***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poff et al. (U.S. Patent 6,123,667).

Poff et al. discloses a sealant prepolymer comprising 20% of 35,000 MW PEG with trimethylene carbonate linkages and acrylate end caps (See Example, col. 11), and teaches that the polymerizable monomers are in solution (See col. 8, lines 29-45). Thus the patent provides a polymerizable macromer comprising a PAG region and one or more reactive groups, which react to form polymeric structures, as claimed in claims 1 and 4-7.

With regard to the mixture of the polymerizable monomer with a PIP, Poff et al. teaches that the adhesive of the invention may include hyaluronic acid (See col. 10, lines 1-11), thus the patent contemplates a mixture of said polymerizable macromer with a PIP, and specifically hyaluronic acid, as claimed in claims 1-3.

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Poff et al. is silent with regard to the viscosity of the composition, however, it is the view of the examiner that the composition contemplated by the prior art would be capable of having a viscosity as claimed by Applicant, in view of the fact that it comprises a mixture of a macromer and PIP, as claimed in the instant application.

With respect to claim 8, Poff et al. provides a composition comprising 20% of the PAG-macromer (See Example), thus the amount of the PAG-macromer disclosed by the prior art is within the range claimed by Applicant. The patent is silent with regard to the amount of hyaluronic acid in the mixture of the invention, however, the artisan skilled in the art would have been able to determine the desired amount of hyaluronic acid by routine experimentation.

Regarding the method claimed in claim 9, Poff et al. provides a method for forming a sealant gel comprising forming an aqueous solution of the sealant prepolymer, applying the solution onto a mesh/tissue surface and polymerizing the solution to form a gel (See Example, col. 11). Poff et al. is deficient in the sense that the method recited in the example does not include a PIP, however, the patent provides the general teachings that the adhesive may be mixed with hyaluronic acid (See col. 10, lines 1-11). Poff et al. is silent with regard to the viscosity of the composition, however, it is the view of the examiner that the composition contemplated by the prior art would be capable of having a viscosity as claimed by Applicant, in view of the fact that it comprises a mixture of a macromer and PIP, as claimed in the instant application.

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With respect to claim 10, Poff et al. provides a composition comprising 20% of the PAG-macromer (See Example), thus the amount of the PAG-macromer disclosed by the prior art is within the range claimed by Applicant. The patent is silent with regard to the amount of hyaluronic acid in the mixture of the invention, however, the artisan skilled in the art would have been able to determine the desired amount of hyaluronic acid by routine experimentation.

Regarding claim 11, Poff et al. teaches that the adhesive of the invention may contain a biologically active agent, such as drugs (See col. 10, lines 1-38).

With regard to the PIP claimed in claims 12 and 13, Poff et al. teaches that the adhesive of the invention may include hyaluronic acid (See col. 10, lines 1-11), thus the patent contemplates a mixture of said polymerizable macromer with a PIP, and specifically hyaluronic acid, as claimed by Applicant.

With respect to claims 14, 21 and 22, the PAG-macromer disclosed by Poff et al. comprises trimethylene carbonate regions, which are biodegradable regions as claimed in claim 14, and multiple acrylate groups (See Example, col. 11).

Regarding claim 23, Poff et al. includes the step of applying two 20-sec pulses of visible light to the prepolymer to form the gel (See Example, col. 11).

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With regard to claims 15-20, Poff et al. provides for the use of the compositions and gels of the invention as tissue sealants and adhesives for application of implants (See Example, col. 11) and for the delivery of bioactive agents (See col. 10, lines 1-38), and teaches that the invention is applicable to any organ and internal tissue, including the eye and muscular tissues (See col. 10, line 39 to col. 11, line 15).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Poff et al. to device polymeric compositions for use as tissue sealants and method for forming said compositions. The expected result would have been a successful adhesive composition and a successful method for forming said composition. Because of the teachings of Poff et al., that the prepolymer compositions may be in solution and include hyaluronic acid and bioactive agents, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant application would be successful in providing tissue coatings and delivering bioactive agents. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Response to Arguments***

3. Applicant's arguments filed on February 24, 2004 have been fully considered but they are not persuasive.
4. Applicant argues that Poff et al. only teaches the presence of hyaluronic acid with regard to tissue-affixing articles or patches, and does not teach or suggest the formation of solutions. In

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response to said argument, it is noted that Poff et al. teaches that the polymerizable monomers are in solution (See col. 8, lines 29-45) and provides a method comprising forming an aqueous solution of the sealant prepolymer, applying the solution onto a mesh/tissue surface and polymerizing the solution to form a gel (See Example, col. 11). Additionally, Poff et al. teaches that the prepolymer of the invention may include hyaluronic acid (See col. 10, lines 1-11), thus the patent contemplates a mixture of said polymerizable macromer with a PIP, and specifically hyaluronic acid. Therefore it would have been obvious to one of the ordinary skill in the art to provide the PIP in solution, so that the PIP solution could be mixed with the PAG solution disclosed by the prior art.

5. In response to Applicant's argument, that Poff et al. does not teach the use of a specific amount of HA sufficient to increase the viscosity of the mixture to be greater than the sum of the viscosities of the components, the burden is shifted to Applicant to show that the HA disclosed by the prior art would not be capable of increasing the viscosity of the mixture as claimed by Applicant.

### ***Conclusion***

6. Claims 1-23 stand rejected.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 571-272-0592. The examiner can normally be reached on Monday through Thursday, 8:30AM-7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*sn83*

April 22, 2004

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